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09/807,836	02/11/2002	Henry Daniell	1466-PCT-US-00	7487
7590	06/10/2004		EXAMINER	
Schnader Harrison Segal & Lewis IP Department 36th Floor 1600 Market Street Philadelphia, PA 19103			KUBELIK, ANNE R	
			ART UNIT	PAPER NUMBER
			1638	

DATE MAILED: 06/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/807,836

Applicant(s)

DANIELL ET AL.

Examiner

Anne R. Kubelik

Art Unit

1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 05 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-43 is/are pending in the application.
- 4a) Of the above claim(s) 6,7 and 11-19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 8,9,20-43 and 105 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 19 April 2001 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>5/10/04, 5/9/01</u> | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. Applicant's election of Group VI (claims 20-22 and 33-38 and claims 1-5, 8-9, 23-33, 39 and 41-43 to the extent they read on drawn to a plastid transformation vector encoding trehalose-6-phosphate synthase in the response filed 5 April 2004 is acknowledged. Because Applicant did not distinctly and specifically point out errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Because art was found on plastid transformation vectors encoding both trehalose-6-phosphate synthase and trehalose-6-phosphate phosphatase, the restriction between these two sequences is withdrawn. Claims 20-22, 36-38 and 40 were inadvertently omitted from the restriction; as they belong to the elected group, they will be examined. The rest of the restriction is made FINAL.

Claims 6-7 and 11-19 are withdrawn from consideration, as being drawn to non-elected inventions. Claims 1-5, 8-9 and 20-43 are examined to the extent they read on vectors encoding trehalose-6-phosphate synthase and trehalose-6-phosphate phosphatase.

2. The drawings are objected to because no details can be made out in Figures 4-6 and 9.

3. The abstract is not descriptive of the instant invention, which is a method of producing drought resistant plants and plants by transformation with the plastid transformation vector encoding trehalose-6-phosphate synthase or trehalose-6-phosphate phosphatase and plants and seeds thereby produced. A new abstract is required that is clearly indicative of the invention to which the claims are directed. The abstract of the disclosure should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

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4. The title of the invention is not descriptive of the instant invention, as above. A new title is required that is clearly indicative of the invention to which the claims are directed. Note that titles can be up to 500 characters long.

5. The Nuccio et al and Rathinasabapathi et al references cited in the IDS filed 10 May 2004 were not sent, and were thus crossed out on the signed form.

### *Claim Objections*

6. Claims 4-5, 8-9 and 20-32 are objected to because of the following informalities:

In claims 4, 8-9, 20-22 and 24, a comma should be inserted before "wherein".

Claims 5, 8, 20 and 25-32 start with in improper article.

In claims 9 and 23, there is an improper article before "group" in lines 1 and 2, respectively.

In claim 23, line 2, "any one of claims 3" should be replaced with --claim 3--.

In claim 25, line 2, "display" should be plural.

In claims 30-31, line 2, --consisting-- should be inserted after "group".

### *Claim Rejections - 35 USC § 112*

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-5, 8-9 and 20-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was

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not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a multitude of plastid transformation vectors encoding any osmoprotectant. The claims are also drawn to vectors comprising plastid sequences conserved in the plastid genomes of different plastid species. In contrast, the specification only describes a plastid transformation vector pCtTPS1, which comprises the *S. cerevisiae* TPS1 gene, and a portion of the tobacco plastid genome. Applicant does not describe other nucleic acids encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

Hence, Applicant has not, in fact, described plastid transformation vectors encoding a osmoprotectant within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

9. Claims 1-5, 8-9 and 20-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing drought resistant plants and plants by transformation with the plastid transformation vector pCtTPS1 and plants and seeds thereby produced, does not reasonably provide enablement for any "5' part of the plastid DNA sequence inclusive of a ... spacer sequence", a promoter operable in plastids, a selectable marker sequence, a DNA sequence encoding any osmoprotectant, a restriction site, a transcription

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termination region, and any “3’ part of the plastid DNA sequence inclusive of a ... spacer sequence”; methods of producing drought resistant plants and plants and seeds thereby produced. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to plastid transformation vectors comprising any “5’ part of the plastid DNA sequence inclusive of a ... spacer sequence”, a promoter operable in plastids, a selectable marker sequence, a DNA sequence encoding any osmoprotectant, a restriction site, a transcription termination region, and any “3’ part of the plastid DNA sequence inclusive of a ... spacer sequence”; methods of producing drought resistant plants and plants and seeds thereby produced. The methods for producing drought resistant plants include selection on PEG.

The instant specification, however, only provides guidance for expression of yeast TPS1 (which encodes trehalose-6-phosphate synthase) in *E. coli* (pg 11), generation of nuclear and chloroplast transformed tobacco (pg 16-18), analysis of expression of yeast TPS1 in the transformed tobacco plants (pg 11-15), analysis of drought tolerance in those plants (pg 15-16). Nuclear transformed plants were stunted and sterile, while chloroplast transformed plants were normal appearing.

The instant specification fails to provide guidance for plastid transformation vectors comprising any osmoprotectant. The instant specification fails to provide guidance for plastid DNA sequences conserved in different plant species. The instant specification also fails to provide guidance for selection of transformants on PEG.

Lee et al (2003, Mole. Breed. 11:1-13) teach that the E. coli otaA gene was not available for their investigation, which is the same as that described in the instant specification (pg 5, left column, paragraph 3). Thus, the specification is not enabled for use of the E. coli otaA gene in the vectors.

Thus, undue experimentation would have been required by one skilled in the art to develop and evaluate methods for producing drought resistant plants and plants by transformation with a plastid transformation vector encoding any osmoprotectant and plants and seeds thereby produced.

Given the claim breath, unpredictability in the art, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-5, 8-9 and 20-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

Claims 1-2 are indefinite in their recitation of the phrase starting with “which comprises” in line 2. It is unclear what the phrase is intended to modify - -stress tolerance? genome? vector? By position in the claim it modifies “stress tolerance”. If Applicant wishes it to modify “vector”, “which” should be replaced with --, wherein the vector--.

Claim 1 lacks antecedent basis for the limitation “said plastid” in line 4.

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Claim 1, lines 3-4, claim 2, lines 3-4, claim 33, lines 3-4, and claim 36, lines 4-5, are indefinite in their recitation of “a 5’ part of the plastid DNA sequence inclusive of a ... spacer sequence”. Plastid genomes are circular, so plastid sequences cannot be 5’ unless a relative position in the circle is given. Additionally, it is unclear what the spacer sequence is - some portion of a plastid genome? Some other sequence? The claims also lack antecedent basis for the limitation “the plastid DNA sequence. Claim 1, line 7, claim 2, lines 7-8, claim 33, lines 7-8, and claim 36, lines 9-10, are similarly indefinite in their recitation of “a 3’ part of the plastid DNA sequence inclusive of a ... spacer sequence”.

Claim 2 lacks antecedent basis for the limitation “said plastid” in line 5.

Claim 2, lines 4 and 8, claim 33, lines 4 and 9, and claim 36, line 5 and 10, are indefinite in their recitation of “conserved”. The level of identity that constitutes “conserved” in the sequences among the different plants species is unclear.

Claim 2 is indefinite in its recitation of “a heterologous target DNA sequence” in lines 6-7. Target DNA sequences for a vector would normally be a sequence in the genome into which the plastid vector is transformed; thus, it is unclear what it means for a vector to have a restriction site for such a sequence.

Claim 3 is indefinite in its recitation of the phrase starting with “that is inserted”. It is unclear what the phrase is intended to modify - “molecule of interest? DNA sequence? vector? By position in the claim it modifies “molecule of interest”.

Claim 3 lacks antecedent basis for the limitation “the restriction sites” in line 2.

It is unclear in claim 5 where the ribosome binding site and the 5’ UTR are located relative to the other components of the vector. It is also unclear what they enhance expression of.



Claim 8 is indefinite for being dependent upon a non-elected claim. Additionally, TSP1, etc., are genes, not sugars, and thus do not further define "trehalose". Lastly "TSP1" should be replaced with --TSP1--.

Claim 9 is indefinite because TSP1 is a gene, not an osmoprotectant. While it may encode an enzyme that produces an osmoprotectant, it is not an osmoprotectant itself, and as such does not further define "osmoprotectant".

Claim 20 is indefinite in its recitation of "at least one DNA". It is unclear where this DNA is located relative to the other components of the vector.

Claim 23 lacks antecedent basis for the limitation "the untransformed plant" in line 3.

It is unclear in claim 32 how a plant can be all of tobacco, tomato, potato, rice, Brassica, cotton, maize and soybean.

Claim 33, line 2, and claim 36, lines 2-3, are indefinite in their recitation of "the plastid of plant species that are susceptible to ... stress". Do all these plant species share a single plastid? Should the phrase be replaced with --a plastid of a plant species that is susceptible to ... stress--?

Claim 33 is indefinite in its recitation of "DNA sequence encoding a gene" in line 5 and claim 36 is indefinite in its recitation of "DNA sequence encoding the ... gene". DNAs encode RNAs or proteins, they do not encode genes, although they may comprise them.

Claims 34 and 37 lack antecedent basis for the limitation "said plant" in lines 1-2.

Claims 34 and 37 are indefinite in their recitation of "an effective amount of ... (PEG) for selection". It is unclear what amount of PEG is effective, and what the plants are selected for.

Claims 35 and 38 lack antecedent basis for the limitation "the selected transformed plant cells".

Claim 36 lacks antecedent basis for the limitation "the Yeast T6P synthase (TSP) gene".

Claim 38 lacks antecedent basis for the limitation "the selected transformed plant cells" in line 2.

Claim 41 lacks antecedent basis for the limitation "The methods of claim 32" as claim 32 is not a method. Additionally, "methods" should be singular.

Claim 42 lacks antecedent basis for the limitation "the intergenic spacer 2 region ... genes" in lines 2-3.

Claim 43 lacks antecedent basis for the limitation "the spacer region" in line 1.

### ***Claim Rejections - 35 USC § 102***

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

13. Claims 1-2, 4-5, 20-21, 23-33 and 39-41 are rejected under 35 U.S.C. 102(e) as being anticipated by Lebel et al (US Patent 6,686,516, filed March 1998, see provisional application 60/077,665).

Lebel et al teach a plastid transformation vector comprising a "a 5' part of the plastid DNA sequence inclusive of a ... spacer sequence" (16S rRNA, trnV and aadA in the pPRV111a vector), a promoter operable in plastids (clpP), a 5' UTR (clpP 5' UTR), a selectable marker sequence (otsA), a DNA sequence encoding an osmoprotectant (otsB), a restriction site (XbaI), a

transcription termination region (rps16 3' UTR), and "a 3' part of the plastid DNA sequence inclusive of a ... spacer sequence" (rps7/12 and vector sequences in the pPRV111a vector); methods of producing drought resistant plants and tobacco, potato and maize plants and seeds thereby produced (column 42, line 26, to column 50, line 52). Tobacco would be edible for a mammal. The vector would be "universal" and the a 5' and 3' parts of the plastid DNA sequence inclusive of a ... spacer sequence would be "conserved" in different plant species. The transformed plants would be more tolerant drought than non-transformed plants. The otsA gene could also be considered the DNA conferring osmoprotection and the otsB gene could be a DNA encoding a molecule of interest.

***Claim Rejections - 35 USC § 103***

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

15. Claims 1-5, 8-9, 20-33, 36 and 39-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lebel et al (US Patent 6,686,516, filed March 1998, see provisional application 60/077,665).

The claims are drawn to a plastid transformation vector comprising a "a 5' part of the plastid DNA sequence inclusive of a ... spacer sequence", a light-inducible promoter operable in plastids, a selectable marker sequence, a DNA sequence encoding yeast TPS1, a restriction site, a transcription termination region, and "a 3' part of the plastid DNA sequence inclusive of a ...

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spacer sequence”, methods of producing drought resistant plants and tobacco, potato and maize plants and seeds thereby produced

The teachings of Lebel et al are discussed above. Additionally, Lebel et al suggest using TPS and TPP sequences that are from *E. coli*, yeast or plants (column 15, lines 18-28; claims 2-3). Lebel et al also suggest using the T7 promoter, the psbA promoter, the rbcL promoter, and the 16S rRNA promoter (column 2, lines 51-52; column 5, lines 45-67; column 19, line 12, to column 20, line 59; claim 12); the rbcL promoter is light-induced. Lebel et al do not teach the claimed plastid transformation vectors in which TPS1 or the rbcL promoter is used, or in which additional sequences of interest are inserted after the DNA encoding an osmoprotectant.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to produce drought resistant plants by transformation of plastids with plastid transformation vectors as taught by Lebel et al, and to modify that to use TPS1 or the rbcL promoter in the vectors, to change the order of the trehalose-6-phosphate synthase and trehalose-6-phosphate phosphatase encoding sequences, insert an additional sequence of interest after the DNA encoding an osmoprotectant, or to place the aadA sequence in the same operon as the trehalose-6-phosphate synthase and trehalose-6-phosphate phosphatase encoding sequences. One of ordinary skill in the art would have been motivated to do so because selection of order of the components in a vector and selection of gene and promoter are obvious design choices.

16. Claims 34-35 and 37-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lebel et al (US Patent 6,686,516, filed March 1998, see provisional application 60/077,665) as applied to claims 1-5, 8-9, 20-33, 36 and 39-41 above, and further in view of Smeekens et al (US Patent 5,986,173, filed 1993).

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The claims are drawn to a method for producing drought resistant plants via transformation with a plastid transformation vector encoding an osmoprotectant, wherein selection is on PEG.

The teachings of Lebel et al are discussed above. Lebel et al do not disclose selection of drought-resistant plants on polyethylene glycol (PEG).

Smeekens et al teach selection of drought-resistant plants on PEG (column 14, lines 41-53).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of producing drought resistant plants as taught by Lebel et al, to selection of drought-resistant plants on PEG as described in Smeekens et al. One of ordinary skill in the art would have been motivated to do so because a range of drought stress levels can effectively be mimicked with PEG (Smeekens et al, column 14, lines 41-53)

17. Claims 42-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lebel et al (US Patent 6,686,516, filed March 1998, see provisional application 60/077,665) as applied to claims 1-5, 8-9, 20-33, 36 and 39-41 above, and further in view of Daniell et al (1998, Nature BioTechnol 16:345-348).

The claims are drawn to plastid transformation vectors encoding any osmoprotectant, wherein the vectors comprise the region between tRNA<sup>Ile</sup> and tRNA<sup>Ala</sup> of a chloroplast genome.

The teachings of Lebel et al are discussed above. Lebel et al do not disclose plastid transformation vectors comprising the region between tRNA<sup>Ile</sup> and tRNA<sup>Ala</sup> of a chloroplast genome.

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Daniell et al teach a plastid transformation vector comprising the region between tRNA<sup>Ile</sup> and tRNA<sup>Ala</sup> of a chloroplast genome (pg 346, left column, paragraph 1).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of producing drought resistant plants as taught by Lebel et al, to use the vector described in Daniell et al. One of ordinary skill in the art would have been motivated to do so because Daniell et al asserts that the vector is universal and would work in plants other than tobacco (pg 346, left column, paragraph 1).

### *Conclusion*

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (571) 272-0547.

Anne R. Kubelik, Ph.D.

June 8, 2004



**ANNE KUBELIK  
PATENT EXAMINER**